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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/842,930	04/25/2001	Paul H. Weigel	5820.603	1177

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EXAMINER
SPECTOR, LORRAINE

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 08/16/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 5/28/02

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 19-47 is/are pending in the application.
Of the above, claim(s) 28-31 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 19-27, 32-47 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☒ Claim(s) 19-47 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 10
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

Part III: Detailed Office Action

Restriction Requirement:

The restriction requirement is moot, applicants having canceled all claims to non-elected groups.

Applicant's election of the species SEQ ID NO: 2 and monoclonal antibody 30 in Paper No. 11, filed 5/28/02, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the species election requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 19-27 and 32-47 are drawn to the elected species, and are under consideration. Claims 28/31 are withdrawn from prosecution as being drawn to non-elected species, there being no allowable generic claim.

Formal Matters:

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The claims are directed not to the identification of hyaluronic acid receptors, but to the receptors themselves.

Objections and Rejections under 35 U.S.C. §112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22, 23, 32-41 and 43-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims which recite "a portion", such as claims 37 and 47 are indefinite, as it is not clear how big a portion is envisioned, the claim does not make such clear, and the specification provides no definition of such to breath life and meaning into the claims. Accordingly, the term has been given minimal weight in applying the prior art to the claims.

Claims which recite "an extracellular domain" of HARE are indefinite because the only known species within the metes and bounds of the claim would be a soluble portion of the 175 kD HARE, which is disclosed to have only a single extracellular portion. Accordingly, the use of the indefinite article 'an' is indefinite, as it would appear to imply the presence of multiple such domains.

Claims 22-23 and 32-36 are indefinite because the metes and bounds of monoclonal antibodies which demonstrate an immunological binding characteristic of one or more of the specifically listed antibodies cannot be determined, as the antibodies themselves have not been described in terms of specific immunological binding characteristics, nor have they been shown to be available. Accordingly, the metes and bounds of the claims cannot be determined.

Claims 41 and 43-47 fail to point out with particularity that which applicant sees as the invention. The claims refer to the claimed receptor only by the term "HARE" and a functional limitation. It is known in the art that there are many HA receptors. Applicants have coined the term HARE to designate "hyaluronic acid receptor for endocytosis". While applicants may be their own lexicographer, it is not likely that the two receptors identified in the specification are the only two that are capable of endocytosing HA. Accordingly, the mere recitation of the name HARE in combination with the single functional limitation that the claimed polypeptide bind "at least one of HA, chondroitin and chondroitin sulfate", is insufficient to adequately and particularly point out that which applicant sees as the invention.

The remaining claims are rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19, 21-23, 25-57, 32-36, 37-41 and 43-47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention.

The specification discloses two HAREs, having molecular weights of 175 and 300 kD (HARE 175 and HARE 300). The specification further teaches that both species exist in both rat and human, and adequately describe both, within the requirements of 35 U.S.C. § 112, first paragraph. However, the written description in the specification is not commensurate in scope with claims to any and all mammalian HARE, including (a) HARE 175 and HARE 300 from species other than rat or human, or (b) HARE other than HARE 175 or HARE 300. The descriptions of the two HARE from rat and human do not constitute a description of the genus of 'mammalian' HARE, as there is no characteristic structure known to be conserved, nor is it predictable what the proteins will look like as isolated from other species. With respect to HARE other than HARE 175 or HARE 300, as stated in the above rejection under 35 U.S.C. § 112 second paragraph, it is not predictable that HARE 175 and HARE 300 are the only endocytosing HARE, and the specification has not provided adequate description of the full scope of endocytosing HA receptors. Further, while there is adequate written description of fragments of rat HARE 175 that bind HA, chondroitin or chondroitin sulfate, the written description in the specification is not commensurate in scope with claims to such fragments of human HARE 175, or rat or human HARE 300 (or any fragments of any other HARE, whether from another mammal or of another size). With respect to human HARE 175, the specification states that only a partial clone has been obtained for human HARE 175, missing a portion of the extracellular (binding) domain. Accordingly, as the specification has not described how to make fragments of said receptor non-recombinantly, and does not provide an adequate written description of the receptor at the molecular level to allow the person of ordinary skill in the art to make such recombinantly, the written description of such is inadequate. With respect to fragments of HARE 300 (rat or human) that retain binding activity, the protein is stated to be trimeric; there is no description of what a binding fragment of such a trimeric receptor would be.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry,

whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of the complete rat and human HARE 175 and 300, and fragments of rat HARE 175 referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only complete rat and human HARE 175 and 300, and fragments of rat HARE 175, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 19, 21-23, 25-27, 32-41 and 43-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for complete HARE 175 and 300, and fragments of HARE 175, is not enabling for fragments of HARE 300, from any species, or for HARE having 40, 80 or 90 percent sequence identity with SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of

predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claimed invention is drawn to mammalian HARE, fragments thereof, and compositions comprising such. The state of the prior art, as cited in the rejections below, is that both human and rat 175 and 300 kD HARE were known and isolated, but had not been cloned. HARE 175 was known to be a single protein, and HARE 300 was known to be trimeric. No other HARE from other mammalian species have been isolated or characterized, nor had any functional fragments of HARE been described or isolated. Although the level of skill in the art is high, it is not predictable that one of ordinary skill in the art could make fragments of HARE 300 that retain function, as the receptor is disclosed as being trimeric in nature; it is not accepted in the art that it is routine to make binding fragments of trimeric receptors, without characterization of the functions of the individual subunits and determination of binding activity. Claims to functional fragments of the HARE 300 are thus a mere invitation to experiment to determine how to make such. Similarly, with respect to claims to 'percent identity', the specification as filed provides little guidance as to how the HARE175 might be altered and still retain function, and no guidance at all with respect to HARE 300. The working examples include the isolation of both receptor from natural sources, a complete clone of rat HARE 175, and a partial clone of human HARE 175. There are no working examples of alterations of any HARE receptor. Accordingly, it is concluded that it would require undue experimentation to practice the claimed invention in a manner commensurate in scope with the claims.

Claims 22-23 and 32-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that monoclonal antibodies 28, 30, 54, 154, 159, 174, 235 and 467 are required to practice the claimed invention. The claims require the availability of those antibodies in order to

determine whether a given protein is within the metes and bounds of the claims. As a required element it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. §112, first paragraph, may be satisfied by a deposit of cells producing the recited antibodies. See 37 C.F.R.§1.802.

The specification does not provide a repeatable method for obtaining the antibodies, and it does not appear to be a readily available material. The particular epitopes bound by the antibodies have not been described, such that the antibodies cannot be reproduced. Deposit of cells which produce the antibodies would satisfy the enablement requirements of 35 U.S.C. §112.

If a deposit is made under terms of the Budapest Treaty, then an affidavit or declaration by Applicants or person associated with the patent owner (assignee) who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty *and* that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 C.F.R.§1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or person associated with the patent owner (assignee) who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, should be submitted stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 C.F.R.§1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 C.F.R.§1.809(d) should be added to the specification. See 37 C.F.R.§§ 1.803-1.809 for additional explanation of these requirements.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 19-27 and 41-47 are rejected under 35 U.S.C. 102(a) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over McCourt et al., Hepatology 30:1276, cited by applicants, or Zhou et al., JBC 274(48):33831-33834, also cited by applicants.

Both references disclose purification of rat HARE.

McCourt et al. disclose isolation of two receptors of 200 and 350 kD, which is consistent with the claimed 175-190 and 300 kD receptors, see last full paragraph page 1279, first column. The isolated fractions of McCourt et al. meet the limitation of being 'purified mammalian HARE' as they are purified relative to their naturally obtainable state (see page 49 of the specification wherein this definition is set forth), and also of being compositions, as they were not purified to homogeneity.

Zhou et al. disclose purification and characterization of the rat liver endocytic hyaluronon receptor (title). It is noted that there is overlap between the authorship of Zhou et al. and the inventorship of this application, and that the work described therein is clearly the same as that disclosed and claimed in the instant application.

Both references are silent with respect to amino acid sequence of the isolated receptors and also with respect to binding of particular antibodies thereto. However, in view of the source, properties, and molecular weights of the disclosed receptors, they appear to be consistent with those of the claims. The examiner is unable to determine whether the prior art disclosure possesses the unrecited characteristics or property. With these conditions, where the (product or apparatus or method or product by process) seems to be identical except that the prior art is silent to the characteristic or property claimed, then the burden shifts to applicant to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention. Note the case law of *In re Best* 195 USPQ 430, 433 (CCPA 1977).

Claims 19-27 and 41-47 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Yannariello-Brown et al., Glycobiology 7:15, cited by applicants.

Yannariello-Brown et al. disclose the purification of rat liver sinusoidal endothelial cell hyaluronan receptor (title). At page 15, first column, they disclose that both 175 kDa and 300 kDa receptors were isolated. See page 18 for discussion of fractions having activity; those fractions meet the limitation of being 'purified mammalian HARE' as they are purified relative to their naturally

obtainable state (see page 49 of the specification wherein this definition is set forth), and also of being compositions, as they were not purified to homogeneity.

The Yannariello-Brown reference is silent with respect to amino acid sequence of the isolated receptors and also with respect to binding of particular antibodies thereto. However, in view of the source, properties, and molecular weights of the disclosed receptors, they appear to be consistent with those of the claims. The examiner is unable to determine whether the prior art disclosure possesses the unrecited characteristics or property. With these conditions, where the (product or apparatus or method or product by process) seems to be identical except that the prior art is silent to the characteristic or property claimed, then the burden shifts to applicant to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention. Note the case law of *In re Best* 195 USPQ 430, 433 (CCPA 1977).

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Banerji et al., J. Cell Biology 144(4):789-801, disclose a hyaluronic acid receptor found on lymph vessel endothelium. There is no indication that the receptor endocytoses HA, rather it is stated to that "LYVE-1 sequesters HA on lymph vessel endothelium in vivo", see page 790, first col.

Advisory Information:

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary L. Kunz, at (703)308-4623.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers

should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to (703) 746-5228.

Lorraine Spector, Ph.D.
Primary Examiner